Contents lists available at ScienceDirect

Asian Pacific Journal of Tropical Medicine

journal homepage:www.elsevier.com/locate/apjtm

Document heading

Assessment of compliance to sulfadoxine-pyrimethamine 18 months after phasing out chloroquine in Mkuranga District, Coast region - Tanzania

Stephen ED Nsimba[1*], Phare G Mujinja[2]

[1] *Prospective College of Health & Allied Sciences (CHAS), School Of Medicine, P. O. Box 395, Dodoma, Tanzania-East Africa*
[2] *Muhimbili University of Health and Allied Sciences, School of Public Health & Social Sciences , P. O. Box 65015, Dar-es-Salaam Tanzania*

ARTICLE INFO

Article history:
Received 4 May 2010
Received in revised form 17 May 2010
Accepted 3 June 2010
Available online 20 June 2010

Keywords:
Malaria
Sulfadoxine-pyrimethamine
Complaince
Choroquine

ABSTRACT

Objective: To observe and assess the compliance to sulfadoxine-pyrimethamine (SP) one and a half years after phasing out chloroquine (CQ) in Mkuranga District, Coast region, Tanzania. **Methods:** A randomly controlled baseline community study was conducted in rural areas of Mkuranga district, Tanzania. Semi-structured questionnaire consisted of open-and closed -ended questions including home stocking, home use, last fever episodes and treatment of underfives with malaria using CQ or SP. **Results:** The prevalence of fever or reported fever rate during the last 48 hours by their mothers or guardians was high (70%). Of all 117 blood samples, only 8 children after drug analysis were found to have CQ and 13 had SP concentrations within their blood respectively. None of these blood drug levels were above therapeutic ranges. **Conclusions:** Community interventions are urgently needed in rural communities and should specifically target households nucleus on early malaria fever recognition and provision of recommended antimalarials for the sick underfive children. However, sadly, there was an increase in underweight and undernourishment in the study areas, probably because of malaria in the area and poverty which are associated with poor nutrition in these youngsters.

1. Introduction

Malaria represents a major health and social-economic problems in Tanzania (with a population of 35.6 million people). In Tanzania malaria ranks as number one in terms of morbidity and mortality. Malaria management has remained the mainstay for mitigating complications of mild and severe malaria including convulsions and death especially in underfive children. Unfortunately malaria management in Tanzania has been hampered significantly by rapid development and spread of resistance to first line drugs which began with chloroquine (CQ) and latter to sulphadoxine-pyrimethamine combinations (SP). Because of resistance of *Plasmodium falciparum* (*P. falciparum*) to SP, Tanzania Malaria Control Program has again replaced SP with Artemesin Combination Treatment [artemisinin-based combination therapy(ACT)] in this case the drug of choice is artemesin and lumefantrine fixed combination [artemesinin-lumefantrine(ALU)] from November 2006.

Malaria kills one child every 30 seconds in Sub-Saharan Africa and more than 3 000 chidren under 5 years per day[1,2]. African children under 5 years are chronic victims of malaria, suffering an average of six bouts a year. Fatally afflicted children often die in less than 72 hours after developing symptoms which are not correctly attended or if there are delays of any kind.

About 30% or more of the malarial disease mortality can be avoided if children can be properly diagnosed, treated with correct effective antimalarial drugs, sleep regularly under treated bed nets containing recommended insecticides such as pyrethroids or long lasting insecticide treated nets (LLTNs).

Several studies have shown a high degree of non-compliance to previously used antimalarials (such as CQ). Unless the barriers and influencing factors are elucidated and addressed, new more effective drugs such as ACT could lead to ineffective treatment and resistance. It is known that over half of caretakers practice self medication when their children suffer from fever[3,4]. This practice may expose parasites to sub-therapeutic doses of ACT with consequences of developing Plasmodium resistance and increasing morbidity and mortality due to malaria. Furthermore, as ACT is expensive and if resistance develops then sub-African countries will have no other better drug options as these countries can not afford more expensive drugs and if this happens it will be catastrophic to most people living in malaria endemic countries. Thus, there is a need to preserve the shelf-life of ACT to delay resistance.

Even though resistance to antimalarial drug is posing major problems, malaria is still a curable and preventable disease, not an inevitable burden. Thus, it is fundamental to control malaria by the case management through early diagnosis, prompt and correct treatment in sub-Saharan countries including Tanzania.

It is therefore, a basic right of the affected populations to

*Corresponding author: Dr Stephen E.D. Nsimba, DDS, MSc, PhD, Prospective College of Health & Allied Sciences (CHAS), School of Medicine,University of Dodoma, P. O. Box 395, Dodoma, Tanzania, East Africa.
Tel: 255-22-713-318113
Fax: 255-26-2310005
E-mail: nsimbastephen@yahoo.co.uk

have access to affordable, safe and efficacious antimalarials. Furthermore, antimalarials need to be available wherever malaria occurs. Children and pregnant women, on whom malaria has its greatest impact in most of the world are especially important and should be targeted.

In many countries of sub-Saharan Africa (SSA) most cases of malaria are diagnosed presumptively based on fever or body hotness and are treated at home by private sector or traditional healers. The treatment offered is often incomplete and irrational through self treatment or self-medication. Thus, rational use of antimalarials can improve medication compliance. Everyone including community members within households should take the responsibility of malaria control and contribute to it. This is only possible if their awareness, perceptions and attitudes can be raised through educational interventions about malaria prevention and rational antimalarial drug use campaigns.

2. Materials and methods

The study was carried out in Mkuranga district, Coast region of Tanzania mainland, where malaria is endemic, from January to April 2003. The peak malaria season occurs in the months of November and June every year.

A total of 1 960 mothers/guardians from which 1 928 children aged 6-59 months where obtained and included in the baseline survey. The demographic profiles of mothers/guardians were:the mean age was 28 years, 55% had no education, 45% had primary education and only 1% had secondary education. Whereas, 53% of children under 5 years were females and 47% were males.

The administrative structure of the district formed the basis for a 3 stage stratified sampling procedure which was used for selecting wards, villages and households. A total of 10 villages out of 20 were randomly selected during this baseline survey. A complete list of wards, villages and households were obtained from the District Planning Officer (DPO) of Mkuranga District, Coast region.

2.1. Data and blood sample collection

Semi-structured questionnaire consisted of open and closed ended questions including home stocking, home use, last fever episodes and treatment practices of underfives with malaria using CQ or SP. The questionnaires were translated into Swahili language and were pre-tested. All mothers of underfive childrenhad interviews in these 10 study villages. The recall period was 2 weeks.

After obtaining verbal consent from mothers or guardians, in every household with one child under five, the capillary blood sample was collected from every fifth child enrolled in the household survey. If a household had more than one children under five, the one who had suffered the most recent fever episode was selected to be taken capillary whole blood sample. Two separate settings of 100 μL blood samples were taken from the same child. A total of 200 μL of blood was taken for analysis of CQ and SP for each child. Blood samples were taken from a total of 117 children through a finger prick. All blood samples were dried on filter paper and analysed for determination of CQ and SP blood drug concentrations using a high performance liquid chromatography (HPLC).

2.2. Data analysis

The results of questionnaire were analysed using software (Stat Soft Inc. Tulse USA). And the blood samples were analysed with HPLC methods for CQ and SP[5]. The accuracy for CQ was measured at 375 nm with a coefficient variation (CV) of 5.3% and accuracy at 451 μM with a CV of 8.9% for sulfadoxine method. The limit of determination was 100 nM for CQ and 25 μM for sulfadoxine, respectively.

2.3. Laboratory investigations

Thick and thin blood smears were taken and Giemsa stained for detection and determination of malaria parasites. The numbers of asexual parasites were counted against 200 white blood cells (WBCs) in thick films. A blood film was considered negative when examination of 500 WBC fields did not show the presence of asexual forms of *P. falciparum*.

2.4. Ethical approval

Participation was voluntary and informed consent was obtained from all households. Ethical approval was obtained from the Tanzania Commission for Science and Technology (COSTECH)-Dar-es-Salaam, Tanzania, and also obtained from the Mkuranga district, Coast region administrative authorities, ward secretaries and leaders of the villages and harmlets. Community consent was sought during village meetings in all study villages and hamlets. During the following visits to individual households, caretakers were asked for their oral consent after receiving detailed information from the study physician about all risks and benefits of the study. They were informed that they could withdraw from the study at any time and without disadvantage.

3. Results

A total of 53% of the children were females and the average age in months for them was 29.6. And 47% of the children were males and the average age in months for them was 30.0 years old. The average age of mothers was 28.1 years old. 54.5% of the mothers or guardians were not educated, 44.5% with primary education and only 1.0% of them with secondary education.

The rate of fever or reported fever of children during the last 48 hours by their mothers or guardians was 70%. 90% of the children were undernourished during the study period.However, only 8 children out of 117 were found to have malaria parasites and most of them had normal body temperature of 36.7 ℃.

Drug analysis showed out of these 117 samples only 8 children were found to have CQ and 13 had SP concentrations within their blood respectively. However, none of these blood drug levels were above therapeutic ranges. At baseline, 26% of the study children had *P. falciparum* parasites detected in their blood smears.

4. Discussion

Malaria is a major public health and socio-economic problem in sub-Saharan countries including Tanzania. It is estimated that every year 300 to 500 million clinical cases of malaria occur[6], and about one million deaths result as a direct consequence of infection with *P. falciparum*[7].

Our study findings show that malaria is common in the study area and it is highly reported by mothers/guardians. Since malaria is common in the area mothers/guardians over-reported the use of antimalarials like SP, but when blood analysis was done all (13) under fives children had sub-therapeutic drug levels of SP and CQ, respectively. Use of sub-therapeutic antimalarial doses has been reported to favour development of CQ drug resistance by parasites[8]. That means either they were not knowledgeable, and the new drug by then (SP) was not yet popular and hence not used frequently. People did not like that drug and hence

used other antimalarials besides SP or did not remember of what kind of drugs they had administered within two weeks. It has been reported from the same study region that SP was negatively perceived by some community members within households when it was 8 months old after introduction in Kibaha district[9].

Unfortunately, we never asked for the other drug alternatives they might have used at that time. It is quite clear that CQ was phased out by the Ministry of Health in July, 2001 and hence CQ was not in the market. Furthermore, most children were undernourished and underweight. Poor nutrition among children makes them prone to infections and their body immune system is weak because they are not fed with nutritious foods. Apart from being prone to infections, both poor nutrition and infections affect children's growth.

It is reported that malaria situation is deteriorating every year in Tanzania[10], as the disease burden increases[1], in relation to the malaria related mortality. Children under the age of five and pregnant women are subject to more episodes of clinical malaria, cerebral malaria, anaemia[11], leading to high mortality rate[12]. This situation has been worsened by the development and widespread of resistance of *P. falciparum* to CQ and the declining efficacy of SP that has severely compromised effective treatment and malaria control programs. Despite these drawbacks, SP is still used for intermittent malaria treatment for pregnant women (IPT_p) and infants (IPTi) in Tanzania mainland[13], Kenya[14] and Malawi[8].

In holo-endemic areas of Tanzania, early malaria diagnosis, correct and prompt effective treatment remains the mainstay of malaria control strategy[15]. Thus there is a strong need for improved understanding of how to optimize malaria treatment policies as to prevent/minimize development and spread of drug resistant malaria including monitoring side effects related to any newly introduced antimalarial drugs like ALU therapy in Tanzania. As drug failure and drug related effects may compromise compliance.

Fixed combination ACT, is a new strategy for malaria treatment after phasing out SP in Tanzania and other sub-Saharan countries. The effectiveness of ACT is based on the hypothesis that two or more components of different mechanisms of action protect each other from development of resistance, simultaneously enhancing the efficacy and promoting compliance. However, irrational use of drugs within households/rural communities in terms of taking inadequate doses, and sometimes not completing doses when patients felt better are some of the factors which could encourage selection of Plasmodium resistance strains to any newly developed and introduced antimalarial including ACT[4,16]. Lack of diagnostic equipment like microscopes and reagents for the diagnosis of malaria often lack in dispensaries and health centers which cater for the health care of the majority of Tanzanians[4].

In order to protect the life span of a new antimalarial drugs, such as ACT, or popularly known as ALU which has a complex regimen as compared to its predecessor SP which was a single dose administered by directly observed therapy(DOT), improving education of patients especially mothers/guardians of underfive children within rural communities/households about rational use of antimalarials including doses, duration of treatment and consequences of incompleting doses is important. The impact of this strategy will be evaluated by assessing malaria morbidity and mortality in the study areas and compared to control areas where no such educational approach is made. Once such interventions are made and if it is found to have positive impact then the National Malaria Control Program within the Ministry of Heath should scale up country wide.

Thus, community interventions are urgently needed in rural communities and should specifically target the households nucleus on early malaria fever recognition and provision of correct recommended antimalarials for the sick underfive children. However, sadly there was an increase in underweight and undernourishment in our study areas. This can be explained by presence of malaria in the area and poverty which is associated with poor nutrition in these underfive children.

Conflict of interest statement

We declare that we have no conflict of interest.

Acknowledgements

The authors would like to thank Mr James Fulgence from the Department of Clinical Pharmacology and Mr Membi -Department of Parasitology, Muhimbili University of Health & Allied Sciences, Tanzania for assistance of capillary blood sample collection and Blood slide collection from our study children. Furthermore, special thanks should go to our mothers/guardians of our underfiv children for willingly participating in the study. Village, ward leaders and district authorities for allowing us undertake this study in their area. Thanks so much to the European Union (EU), for granting us financial support to undertake this study.

References

[1]World Health Organization. *Factsheet No. 94*. Geneva: WHO; 1998.
[2]MoH-Tanzania. *Morbidity and mortality statistics: Health statistics abstract*. Health Information and Research Section, Planning & Policy Department, Ministry of Health, Tanzania; 1999.
[3]Nsungwa-Sabiiti J, TomsonG, Pariyo G, Ogwal-Okeng J, Peterson S. Community effectiveness of malaria treatment in Uganda--a long way to Abuja targets. *Ann Trop Paediatr* 2005; **25**: 91-100.
[4]Nsimba SED, Massele AY, Eriksen J, Gustafsson LL, Tomson G, Warsame M. Case management of malaria in under-fives at primary health care facilities in a Tanzanian district. *Trop Med & Int Health* 2002; **7**: 201-9.
[5]Bergqvist Y, Hjelm E, Rombo L. Sulfadoxine assay using capillary blood samples dried on filter paper--suitable for monitoring of blood concentrations in the field. *Ther Drug Monit* 1987; **9**: 203-7.
[6]Breman J. The ears of the hippopotamus: manifestations, determinants, and estimates of the malaria burden. *Am J Trop Med Hyg* 2001; **64**S: 1-11.
[7]Snow RW, Craig M, Deichmann U, Marsh K. Estimating mortality, morbidity and disability due to malaria among Africa's non-pregnant population. *Bull World Health Org* 1999; **77**: 624-40.
[8]Bloland PB, Ettling M. Making malaria-treatment policy in the face of drug resistance. *Ann Trop Med & Parasitol* 1999; **93**: 5-23.
[9]Nsimba SED. How sulfadoxine-pyrimethamine (SP) was perceived in some rural communities after phasing out chloroquine (CQ) as a first-line drug for uncomplicated malaria in Tanzania : lessons to learn towards moving from monotherapy to fixed combination therapy. *J Ethnobiol & Ethnomed* 2006; **2**: 5-12.
[10]Greenwood B, Mutabingwa T. Malaria in 2002. *Nature* 2002; **415**: 670-2.
[11]Ekvall H, Premji Z, Bjorkman A. Chloroquine treatment for uncomplicated childhood malaria in an area with drug resistance: early treatment failure aggravates anaemia. *Trans R Soc Trop Med Hyg* 1998; **92:** 556-60.
[12]Snow RW, Trape JF, Marsh K. The past, present and future of childhood malaria mortality in Africa. *Trends Parasitol* 2001; **17**: 593-7.
[13]Ministry of Health. *National Guidelines for Malaria*. Dar-es-Salaam, Tanzania; 2000.
[14]Shretta R, Omumbo J, Rapuoda B, Snow RW. Using evidence to Change antimalarial drug policy in Kenya. *Trop Med & Int Health* 2000; **5**: 755-64.
[15]Goodman CA, Coleman PG, Mills AJ. Cost-effectiveness of malaria control in sub-Saharan Africa. *Lancet* 1999; **354**: 378-85.
[16]White NJ, Nosten F, Looareesuwan S, Watkins WM, Marsh K, Snow RW, et al. Averting a malaria disaster. *Lancet* 1999; **353**: 1965-67.